

10/758241

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STRUCTURE FILE UPDATES: 17 MAR 2008 HIGHEST RN 1008496-49-8
DICTIONARY FILE UPDATES: 17 MAR 2008 HIGHEST RN 1008496-49-8

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

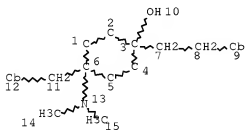
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REGISTRY includes numerically searchable data for experimental and
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<http://www.cas.org/support/stngen/stndoc/properties.html>

L1

STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L2 14 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 624 ITERATIONS 14 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 10:59:13 ON 18 MAR 2008
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FILE COVERS 1907 - 18 Mar 2008 VOL 148 ISS 12
 FILE LAST UPDATED: 17 Mar 2008 (20080317/ED)

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 They are available for your review at:

<http://www.cas.org/infopolicy.html>

L3 1 L2

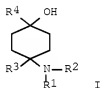
L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:76742 CAPLUS Full-text
 DOCUMENT NUMBER: 138:137023
 TITLE: Preparation of 4-amino-4-(arylalkyl)cyclohexanols
 as ORL1 receptor ligands for treatment of pain
 INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-heinrich;
 Koegel, Babette-yvonne; Wnendt, Stephan
 PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
 SOURCE: PCT Int. Appl., 75 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008371	A1	20030130	WO 2002-EP7849	20020715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10135635	A1	20030206	DE 2001-10135635	20010717
DE 10135637	A1	20030206	DE 2001-10135637	20010717
CA 2453843	A1	20030130	CA 2002-2453843	20020715
AU 2002328894	A1	20030303	AU 2002-328894	20020715
AU 2002328894	B2	20070614		
EP 1406859	A1	20040414	EP 2002-764691	20020715
EP 1406859	B1	20080102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011223	A	20040810	BR 2002-11223	20020715
HU 2004000207	A2	20040830	HU 2004-207	20020715
CN 1555355	A	20041215	CN 2002-817915	20020715
JP 2005504742	T	20050217	JP 2003-513932	20020715
NZ 531112	A	20050930	NZ 2002-531112	20020715
AT 382601	T	20080115	AT 2002-764691	20020715

10/758241

RU 2315750	C2	20080127	RU 2004-104628	20020715
MX 2004PA00272	A	20040504	MX 2004-PA272	20040109
NO 2004000162	A	20040311	NO 2004-162	20040114
US 2004214822	A1	20041028	US 2004-758241	20040116
ZA 2004001223	A	20041130	ZA 2004-1223	20040216
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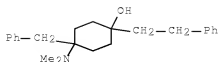
OTHER SOURCE(S): MARPAT 138:137023
GI



AB Title compds. I [wherein R1 and R2 = independently H or (un)substituted (cyclo)alkyl; or NR1R2 = morpholinyl, (un)substituted piperazinyl, pyrrolidinyl, piperidinyl, etc.; R3 = (cyclo)alkyl optionally substituted with cycloalkyl or (hetero)aryl; R4 = (un)substituted cycloalkyl or (hetero)aryl; and racemates, stereoisomers, pharmaceutically acceptable salts, and hydrates thereof] were prepared for treating various indications, especially pain. For example, reaction of 1,4-dioxaspiro[4.5]decan-8-one with dimethylamine•HCl and KCN gave 3-dimethylamino-1,4- dioxaspiro[4.5]decan-8-nitrile. Substitution with benzylmagnesium chloride, conversion to the cyclohexanone, addition of phenethylmagnesium chloride, and recrystn. afforded 4-benzyl-4-dimethylamino-1- phenethylcyclohexanol•HCl. The latter exhibited binding to the ORL1 opioid receptor with Ki of 0.02 μ M and demonstrated analgesic activity in the mouse tail flick test with ED50 of 0.015 mg/kg i.v.

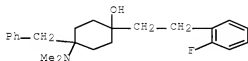
IT 492461-58-2P, 4-Benzyl-4-dimethylamino-1-phenethylcyclohexanol
492461-64-8P, 4-Benzyl-4-dimethylamino-1-[2-(2-fluorophenyl)ethyl]cyclohexanol 492461-66-2P,
4-Benzyl-4-dimethylamino-1-[2-(4-fluorophenyl)ethyl]cyclohexanol
492461-70-8P, 4-Dimethylamino-4-(2-fluorobenzyl)-1-phenethylcyclohexanol 492461-74-2P, 4-Dimethylamino-4-(3-fluorobenzyl)-1-phenethylcyclohexanol 492461-78-6P,
4-Dimethylamino-4-(4-fluorobenzyl)-1-phenethylcyclohexanol
RL: RCT (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(analgesic; preparation of (amino)(arylalkyl)cyclohexanol analgesics starting from dioxaspiro[4.5]decanones, amines, and arylalkylmagnesium chlorides)

RN 492461-58-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(2-phenylethyl)-4-(phenylmethyl)-
(CA INDEX NAME)



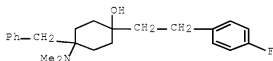
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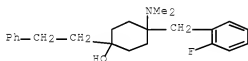
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CN Cyclohexanol, 4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-4-(phenylmethyl)- (CA INDEX NAME)



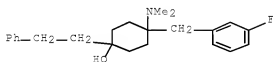
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CN Cyclohexanol, 4-(dimethylamino)-4-[(2-fluorophenyl)methyl]-1-(2-phenylethyl)- (CA INDEX NAME)



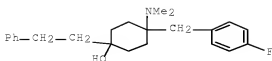
RN 492461-74-2 CAPLUS

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RN 492461-78-6 CAPLUS

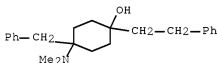
CN Cyclohexanol, 4-(dimethylamino)-4-[(4-fluorophenyl)methyl]-1-(2-phenylethyl)- (CA INDEX NAME)



IT 492461-57-1P, 4-Benzyl-4-dimethylamino-1-phenethylcyclohexanol hydrochloride 492461-63-9P, 4-Benzyl-4-dimethylamino-1-[2-(2-fluorophenyl)ethyl]cyclohexanol hydrochloride 492461-65-1P, 4-Benzyl-4-dimethylamino-1-[2-(4-fluorophenyl)ethyl]cyclohexanol hydrochloride 492461-67-3P, 4-Dimethylamino-4-(2-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-71-9P, 4-Dimethylamino-4-(3-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-75-3P, 4-Dimethylamino-4-(4-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492462-25-6P, 4-Benzyl-4-dimethylamino-1-[2-(3-fluorophenyl)ethyl]cyclohexanol 492462-26-7P, 4-Benzyl-4-dimethylamino-1-[2-(3-fluorophenyl)ethyl]cyclohexanol hydrochloride
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (analgesic; preparation of (amino)(arylalkyl)cyclohexanol analgesics starting from dioxaspiro[4.5]decanones, amines, and arylalkylmagnesium chlorides)

RN 492461-57-1 CAPLUS

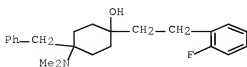
CN Cyclohexanol, 4-(dimethylamino)-1-(2-phenylethyl)-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 492461-63-9 CAPLUS

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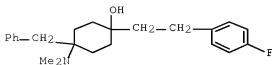


● HCl

RN 492461-65-1 CAPLUS

10/758241

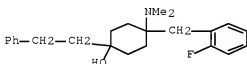
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 492461-67-3 CAPLUS

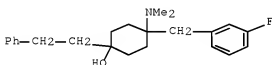
CN Cyclohexanol, 4-(dimethylamino)-4-[(2-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 492461-71-9 CAPLUS

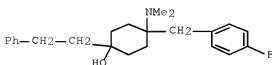
CN Cyclohexanol, 4-(dimethylamino)-4-[(3-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

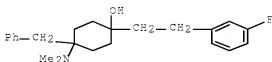
RN 492461-75-3 CAPLUS

CN Cyclohexanol, 4-(dimethylamino)-4-[(4-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)

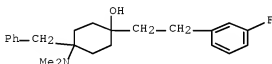


● HCl

RN 492462-25-6 CAPLUS
 CN Cyclohexanol, 4-(dimethylamino)-1-[2-(3-fluorophenyl)ethyl]-4-(phenylmethyl)- (CA INDEX NAME)



RN 492462-26-7 CAPLUS
 CN Cyclohexanol, 4-(dimethylamino)-1-[2-(3-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE COVERS 1907-1966
 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L4 0 L2

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L5 0 L2

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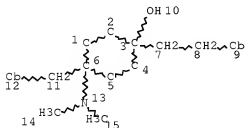
FILE CONTENT: 1961-PRESENT VOL 148 ISS 11 (20080314/ED)
SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987
MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2008027098 31 JAN 2008
DE 102006031752 10 JAN 2008
EP 1881549 23 JAN 2008
JP 2008021517 31 JAN 2008
WO 2008021152 21 FEB 2008
GB 2439172 19 DEC 2007
FR 2903984 25 JAN 2008
RU 2315659 27 JAN 2008
CA 2593150 06 JAN 2008

Expanded G-group definition display now available.

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SLIMITS at an arrow prompt.

L6 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 9 12
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES

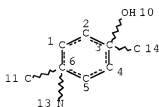
ALL RING(S) ARE ISOLATED

L8 0 SEA FILE=MARPAT SSS FUL L6 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 49148 ITERATIONS
SEARCH TIME: 00.00.22

0 ANSWERS

L9 STR



NODE ATTRIBUTES:

NSPEC IS RC AT 11
 NSPEC IS RC AT 13
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 CONNECT IS X2 RC AT 1
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 CONNECT IS X2 RC AT 4
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 DEFAULT MLEVEL IS ATOM
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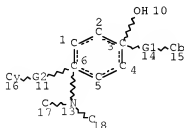
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RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

ECLEVEL IS LIM ON ALL NODES
 ALL RING(S) ARE ISOLATED

L10 (212)SEA FILE=MARPAT SSS FUL L9 (MODIFIED ATTRIBUTES)
L11 STR

REP G1=(0-2) CH2
 REP G2=(0-1) CH2
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 CONNECT IS X2 RC AT 1
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

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 NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

ECLEVEL IS LIM ON ALL NODES
 ALL RING(S) ARE ISOLATED

L12 7 SEA FILE=MARPAT SUB=L10 SSS FUL L11 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 162 ITERATIONS 7 ANSWERS
 SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 11:11:17 ON 18 MAR 2008

L13 7 S L12
 L14 6 S L13 NOT L3

FILE 'MARPAT' ENTERED AT 11:11:36 ON 18 MAR 2008

L15 6 S L14

L15 ANSWER 1 OF 6 MARPAT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 147:357143 MARPAT Full-text
 TITLE: Thioresdoxin and thioresdoxin reductase inhibitors
 INVENTOR(S): Schaus, Scott E.; Eastwood, Erin L.
 PATENT ASSIGNEE(S): Trustees of Boston University, USA
 SOURCE: PCT Int. Appl., 89pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007103273	A2	20070913	WO 2007-US5530	20070302
WO 2007103273	A3	20071122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
PRIORITY APPLN. INFO.:			US 2006-778876P 20060303	

AB The present invention relates to sulfone derivs. and to their use as modulators of the thioredoxin/thioredoxin reductase redox system, including for the treatment and/or prevention of pathophysiol. conditions mediated by thioredoxin/thioredoxin reductase, such as cancer, HIV/ AIDS, Alzheimer's disease, rheumatoid arthritis, and skin disorders. Also provided are pharmaceutical compns. comprising the inventive sulfones. The targets of a novel tetrazole-containing compound, 4-(1-phenyl-1H-tetrazol-5-ylsulfonyl)butanenitrile (PTSB) that inhibited cell growth of A549 lung carcinoma cells, were determined by studying the changes in steady-state gene expression in *Saccharomyces cerevisiae* upon treatment with PTSB using oligonucleotide arrays, the MNI algorithm, and the reverse-engineered network model. Two genes, for thioredoxin reductase and for thioredoxin were identified and then confirmed by a biochem. assay. A library of 36 compds. was designed and developed to include the sulfone and/or the nitrile functionalities and tested in a cancer cell growth inhibition assay.

L15 ANSWER 2 OF 6 MARPAT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 146:168880 MARPAT Full-text
 TITLE: Wrinkle-preventive/ameliorating agents comprising
 α -amino acid derivatives
 INVENTOR(S): Tsunenaga, Makoto; Iwaki, Haruhi; Iida, Toshii;
 Kaminuma, Mikiko; Suetsugu, Masaru; Takada, Keiko;
 Inomata, Shinji
 PATENT ASSIGNEE(S): Shiseido Company, Ltd., Japan
 SOURCE: PCT Int. Appl., 53pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007013662	A1	20070201	WO 2006-JP315248	20060726
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, NG, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: JP 2005-215426 20050726

AB Disclosed is a wrinkle-preventive/ameliorating agent comprising one or more compds. selected from the group consisting of an α -amino acid derivative represented by the general formula, NR₁R₂CHR₃C(=O)OR₄ and a salt thereof, wherein R₁ represents H, CH₃ or CH₂OH; R₂ and R₃ independently represent H, C₁-4-alkyl group, or R₂ and R₃, together with N atom may form a C₄-6 cyclic structure which may have O; and R₄ represents H, C₁-18 alkyl, provided that a situation where one of R₂ and R₃ is a benzyloxycarbonyl group and the other is H does not occur when both R₁ and R₄ represent H. For example, antiwrinkle cream contained sarcosine 20, stearic acid 5, stearyl alc. 4, iso-Pr myristate 18, glycerin monostearate 3, propylene glycol 10, KOH 0.2, preservatives q.s., perfumes q.s., and ion-exchanged water balance to 100 %.

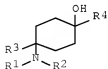
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

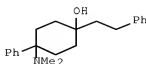
L15 ANSWER 3 OF 6 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 138:136953 MARPAT Full-text
TITLE: Preparation of substituted 4-aminocyclohexanols as
regulators for the nociceptin/orphanin FQ ligand
ORL-1 receptor system
INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-heinrich;
Englberger, Werner; Wnendt, Stephan
PATENT ASSIGNEE(S): Gruenthal GmbH, Germany
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003008370	A1	20030130	WO 2002-EP7842	20020715
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10135636	A1	20030206	DE 2001-10135636	20010717
CA 2453901	A1	20030130	CA 2002-2453901	20020715
AU 2002321215	A1	20030303	AU 2002-321215	20020715
AU 2002321215	B2	20070802		
EP 1406858	A1	20040414	EP 2002-754882	20020715
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
HU 2004001082	A2	20040830	HU 2004-1082	20020715
JP 2004534858	T	20041118	JP 2003-513931	20020715
MX 2004PA00446	A	20040318	MX 2004-PA446	20040115
US 2004236104	A1	20041125	US 2004-758242	20040116
US 7183436	B2	20070227		
PRIORITY APPLN. INFO.:			DE 2001-10135636	20010717
			WO 2002-EP7842	20020715

GI



I



II

AB Title compds. I [R₁-2 = H, alkyl, cycloalkyl, etc.; R₃ = (hetero)aryl; R₄ = cycloalkyl, (hetero)aryl, etc.] are prepared For instance, 1,4-dioxoaspiro[4.5]decan-8-one was converted to 8-dimethylamino-1,4-

dioxaspiro[4.5]decan-8-carbonitrile (MeOH, Me₂NH, KCN). Displacement of this intermediate with phenylmagnesium chloride followed by deprotection and subsequent treatment with phenethylmagnesium chloride results in the formation of II. II has $K_i = 4.4$ nM for the ORL-1 receptor. I are useful for treating pain.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 6 MARPAT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:

136:5907 MARPAT Full-text

TITLE:

Synthesis of aryl-amido-cyclohexane derivatives and their use as NK-1 receptor antagonists

INVENTOR(S):

Castro Pineiro, Jose Luis; Dinnell, Kevin; Elliott, Jason Matthew; Hollingworth, Gregory John; Shaw, Duncan Edward; Swain, Christopher John

PATENT ASSIGNEE(S):

Merck Sharp & Dohme Limited, UK

SOURCE:

PCT Int. Appl., 199 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

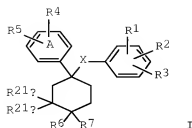
English

FAMILY ACC. NUM. COUNT: 1

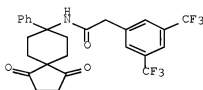
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087838	A1	20011122	WO 2001-GB2145	20010516
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2408849	A1	20011122	CA 2001-2408849	20010516
EP 1286967	A1	20030305	EP 2001-929829	20010516
EP 1286967	B1	20060927		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003533509	T	20031111	JP 2001-584234	20010516
AT 340781	T	20061015	AT 2001-929829	20010516
ES 2273837	T3	20070516	ES 2001-929829	20010516
US 2003236250	A1	20031225	US 2002-276127	20021113
US 7105507	B2	20060912		
PRIORITY APPLN. INFO.:			GB 2000-12240	20000519
			WO 2001-GB2145	20010516

GI



I



II

AB Title compds. I [ring A = Ph or pyridyl; X = linker selected from amido(carbonyl), amino, ester, ether; R1 = OH, (fluoro)alkyl, alkenyl, cycloalkyl, (fluoro)alkoxy, etc.; R2 = H, halo, alkyl, alkoxy or R1-2 with the atom to which they are attached, may form a 5 - 6 membered ring; R3 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, cycloalkyl, CN, etc. or R3 = 5 - 6 membered heterocyclic ring; R4 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, OH, NO2, CN, etc.; R5 = H, halo, (fluoro)alkyl, alkoxy; R6 = H, OH, alkyl; R7 = H, OH, alkylamino, alkylcarboxy, carbocyclyl, C-linked heterocyclyl or heteroaryl or R6-7 together represent :O, :CH-ester, ketal; R21a = H, halo, OH; R21b = H, or R21a-21b = F or together represent :O] were prepared Over 300 synthetic examples were disclosed. For instance, 3,5- bis(trifluoromethyl)benzeneacetic acid was converted to the acid chloride derivative (CH₂Cl₂, ClCOCOC₂Cl, DMF, room temperature, 1 h), and used to acylate 1,4-dioxo-8-phenylspiro[4.5]decan-8-amine (preparation given, dichloroethane, Et₃N, room temperature) to give II as a brown gum in quant. yield. I are neurokinin 1 (NK-1) receptor antagonists (no data). Compds. I are of particular use in the treatment or prevention of depression, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 6 MARPAT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 124:260852 MARPAT [Full-text](#)
 TITLE: Improved Chichibabin aminations of pyridine bases
 INVENTOR(S): Lawin, Phillip B.; Sherman, Angela R.; Grendze, Martin P.
 PATENT ASSIGNEE(S): Reilly Industries, Inc., USA
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9600216	A1	19960104	WO 1995-US8030	19950626

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, DE, EE, FI, GE, HU, IS,
 JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ,
 PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN
 RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
 IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
 MR, NE, SN, TD, TG

IL 114314	A	20001206	IL 1995-114314	19950625
CA 2193236	A1	19960104	CA 1995-2193236	19950626
AU 9529100	A	19960119	AU 1995-29100	19950626
EP 703530	B2	19990325		
EP 766675	A1	19970409	EP 1995-924694	19950626

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,
 PT, SE

BR 9508123	A	19970812	BR 1995-8123	19950626
CN 1156990	A	19970813	CN 1995-194733	19950626
HU 76424	A2	19970828	HU 1996-3557	19950626
HU 217172	B	19991228		
JP 10502089	T	19980224	JP 1996-503374	19950626
RU 2165414	C2	20010420	RU 1997-101086	19950626
IN 183814	A1	20000429	IN 1995-CA744	19950630
US 5808081	A	19980915	US 1996-765281	19961220

PRIORITY APPLN. INFO.:	US 1994-265321	19940624
	US 1995-480440	19950607
	WO 1995-US8030	19950626

OTHER SOURCE(S): CASREACT 124:260852

AB Improved Chichibabin aminations of pyridine bases are described which are conducted under a pressurized gas phase containing ammonia and in the presence of a selected additive [e.g., $\text{RLX}(\text{CH}_2)_n\text{XR}_2$ wherein $\text{X} = \text{S}, \text{O}, \text{NR}_3, \text{CO}_2$; $\text{R}_1 - \text{R}_3 = \text{H}, \text{alkyl}, \text{etc.}$; $n = 0 - 12$] which increases the reaction rate, and also in preferred processes favorably alters the isomer ratios and product yields from the aminations while benefiting product workup and recovery as well. Thus, amination of pyridine in toluene containing NaNH_2 and monoethanolamine gave 2-amino-pyridine. The use of monoethanolamine greatly reduces the reaction time.

L15 ANSWER 6 OF 6 MARPAT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 91:74328 MARPAT Full-text
 TITLE: 4-Aminocyclohexanols, their acylates and acid addition salts

INVENTOR(S): Lednicer, Daniel
 PATENT ASSIGNEE(S): Upjohn Co., USA
 SOURCE: Ger. Offen., 58 pp.
 CODEN: GWXXBX

DOCUMENT TYPE: Patent
 LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2839891	A1	19790412	DE 1978-2839891	19780913
US 4366172	A	19821228	US 1977-837510	19770929
GB 2005266	A	19790419	GB 1978-38272	19780927
GB 2005266	B	19820203		
FR 2404625	A1	19790427	FR 1978-27780	19780928
FR 2404625	B1	19811224		
JP 54059263	A	19790512	JP 1978-120333	19780929
CH 635818	A5	19830429	CH 1978-10157	19780929

PRIORITY APPLN. INFO.:	US 1977-837510	19770929
GI		



AB Aminocyclohexanols I [R = H, R1CO (R1 = C1-3 alkyl); R2 = H, C1-6 aliphatic group, cycloalkylalkyl (optionally unsatd.), (substituted) phenylalkyl; R3, R4 = C1-5 alkyl; R5 = H, halo, OH, C1-3 alkyl in meta or para position] and their physiol. acceptable salts, useful as analgesics (no data) were prepared Thus, 4-hydroxycyclohexanone was successively acetalized with (HOCH2)2, 4-hydroxycyclohexanone ethylene ketal oxidized with CrO3 (91% yield), 1,4-cyclohexanedione mono(ethylene ketal) cyanated with KCN and aminated with Me2NH.HCl (78% yield), nitrile II (R6R6 = OCH2CH2O, R7 = cyano) treated with 4-ClC6H4MgBr (34% yield), phenylcyclohexanone ketal II (R6R6 = OCH2CH2O, R7 = 4-ClC6H4) hydrolyzed with 2N HCl in MeOH (70% yield), and ketone II (R6R6 = O, R7 = 4-ClC6H4) reduced with NaBH4 to give 30% cyclohexanol I (R = R2 = H, R3 = R4 = Me, R5 = 4-Cl).

FILE 'REGISTRY' ENTERED AT 11:14:53 ON 18 MAR 2008

L17 113 SEA ABB=ON PLU=ON ?BENZYL-4-DIMETHYLAMINO?/CNS
L18 21 SEA ABB=ON PLU=ON L16(L)L17

FILE 'CAPLUS' ENTERED AT 11:15:17 ON 18 MAR 2008

L19 3 SEA ABB=ON PLU=ON L18
L20 35 SEA ABB=ON PLU=ON (4(W) (BENZYL OR BZ))(1(W) (DIMETHYLAMINO?
OR DI(W) (METHYLAMINO? OR (ME OR METHYL) (W)AMINO?) OR
DIMETHYL AMINO?)
L21 2 SEA ABB=ON PLU=ON L20(S) (?CYCLOHEXANOL? OR ?CYCLO
HEXANOL?)
L22 2 SEA ABB=ON PLU=ON (L19 OR L21) NOT L3

L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ED Entered STN: 24 Jan 2008

ACCESSION NUMBER: 2008:94964 CAPLUS Full-text

DOCUMENT NUMBER: 148:191845

TITLE: Preparation of cyclohexylindoles as opioid
receptor-like 1 (ORL1) receptor inhibitors
INVENTOR(S): Zemolka, Saskia; Schunk, Stefan; Englberger,
Werner; Koegel, Babette-Yvonne; Linz, Klaus;
Schick, Hans; Sonnenschein, Helmut; Graubaus,
Heinz; Hinze, Claudia

PATENT ASSIGNEE(S): Gruenenthal GmbH, Germany

SOURCE: PCT Int. Appl., 303pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008009415	A2	20080124	WO 2007-EP6325	20070717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,				
CA, CH, CN, CO, CR, CU, CZ, DK, DM, DO, DZ, EC, EE, EG, ES,				
FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,				

10/758241

KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY,
MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM,
SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA,
ZM, ZW

RW: AI, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

DE 102006033109

A1 20080131

DE 2006-102006033109 20060718

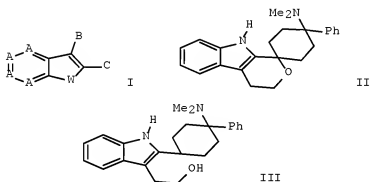
PRIORITY APPLN. INFO.:

DE 2006-102006033109A 20060718

OTHER SOURCE(S):

MARPAT 148:191845

GI



AB Title compds. I [A = N, CR7-10; B, C = H, alkyl, cycloalkyl, etc.; R7, R8, R9, R10 = H, halo, NO2, etc.; W = O, S, NR4, preferably NH; R4 = H, C1-5 alkyl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, tin-mediated reduction of pyranose II gave the citrate salt of claimed indole III. In ORL1 receptor inhibition assays, 6 examples of compds. I exhibited Ki values ranging from 0.0009-3 μ M.

IT 492462-14-3P 492462-23-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(preparation of cyclohexylindoles as opioid receptor-like 1 (ORL1)
receptor inhibitors)

L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

ED Entered STN: 03 Oct 2003

ACCESSION NUMBER: 2003:777742 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:291992

TITLE: Preparation of substituted 4-aminocyclohexanols
for treatment of pain

INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-Heinrich;
Englberger, Werner; Koegel, Babette-Yvonne
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080557	A1	20031002	WO 2003-EP2812	20030318
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10213051	A1	20031030	DE 2002-10213051	20020323
CA 2480038	A1	20031002	CA 2003-2480038	20030318
AU 2003212366	A1	20031008	AU 2003-212366	20030318
EP 1487778	A1	20041222	EP 2003-708253	20030318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526795	T	20050908	JP 2003-578315	20030318
US 2005187220	A1	20050825	US 2004-947551	20040923
US 7211694	B2	20070501		
PRIORITY APPLN. INFO.:			DE 2002-10213051	A 20020323
			WO 2003-EP2812	W 20030318

OTHER SOURCE(S): CASREACT 139:291992; MARPAT 139:291992
GI



- AB Aminocyclohexanols I [R1, R2 = H, (un)substituted aliphatic, cycloalkyl, aryl, heterocyclyl; R1R2 = CH2CH2OCH2CH2, (un)substituted CH2CH2NHCH2CH2, (CH2)3-6; R3 = (un)substituted aliphatic, cycloalkyl, aryl, heterocyclyl; R4 = (un)substituted cycloalkyl, aryl, heterocyclyl] were prepared. Thus, 1,4-dioxaspiro[4.5]decan-8-one was reduced to the alc., o-benzylated, hydrolyzed to the ketone, and treated with Me2NH·HCl and KCN to give 4-benzyl-1-dimethylaminocyclohexanecarbonitrile which was treated with PhMgBr and NH4Cl to give I [R1, R2 = Me, R3 = Ph, R4 = PhCH2] whose diastereomers were separated. The diastereomers had IC50 for ORL-1 binding of 0.069 and 0.40 μM, resp.
- IT 607717-22-6P, 4-Benzyl-4-dimethylaminocyclohexanol.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted 4-aminocyclohexanols for treatment of pain)
- REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR

10/758241

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RE FORMAT

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L23 1 S L21

L23 ANSWER 1 OF 1 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-267985 [26] WPIX
DOC. NO. CPI: C2003-069839 [26]
TITLE: New substituted 4-aminocyclohexanol derivatives, are
ORL1 receptor ligands useful e.g. for treating
anxiety, depression, epilepsy, Alzheimer's disease,
cardiovascular disease or especially pain
DERWENT CLASS: B05
INVENTOR: HENNIES H; HENNIES H H; KOEGEL B; KOEGEL B Y; KOEGEL
B; SUNDERMANN B; WENNDT S
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 99

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003008371	A1	20030130	(200326)*	DE	75[0]	
DE 10135635	A1	20030206	(200326)	DE		
DE 10135637	A1	20030206	(200326)	DE		
EP 1406859	A1	20040414	(200426)	DE		
KR 2004029369	A	20040406	(200451)	KO		
AU 2002328894	A1	20030303	(200452)	EN		
BR 2002011223	A	20040810	(200455)	PT		
HU 2004000207	A2	20040830	(200465)	HU		
US 20040214822	A1	20041028	(200471)	EN		
MX 2004000272	A1	20040501	(200482)	ES		
JP 2005504742	W	20050217	(200513)	JA	115	
CN 1555355	A	20041215	(200519)	ZH		
ZA 2004001223	A	20050223	(200519)	EN	104	
NO 2004000162	A	20040311	(200557)	NO		

10/758241

NZ 531112	A	20050930	(200566)	EN
AU 2002328894	B2	20070614	(200765)	EN
EP 1406859	B1	20080102	(200805)	DE
RU 2315750	C2	20080127	(200810)	RU
DE 50211466	G	20080214	(200813)	DE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003008371	A1	WO 2002-EP7849	20020715
DE 10135635	A1	DE 2001-10135635	20010717
DE 10135637	A1	DE 2001-10135637	20010717
AU 2002328894	A1	AU 2002-328894	20020715
AU 2002328894	B2	AU 2002-328894	20020715
BR 2002011223	A	BR 2002-11223	20020715
CN 1555355	A	CN 2002-817915	20020715
EP 1406859	A1	EP 2002-764691	20020715
EP 1406859	B1	EP 2002-764691	20020715
NZ 531112	A	NZ 2002-531112	20020715
EP 1406859	A1	WO 2002-EP7849	20020715
BR 2002011223	A	WO 2002-EP7849	20020715
HU 2004000207	A2	WO 2002-EP7849	20020715
US 20040214822	A1 Cont of	WO 2002-EP7849	20020715
MX 2004000272	A1	WO 2002-EP7849	20020715
JP 2005504742	W	WO 2002-EP7849	20020715
NO 2004000162	A	WO 2002-EP7849	20020715
NZ 531112	A	WO 2002-EP7849	20020715
EP 1406859	B1	WO 2002-EP7849	20020715
RU 2315750	C2	WO 2002-EP7849	20020715
JP 2005504742	W	JP 2003-513932	20020715
HU 2004000207	A2	HU 2004-207	20020715
RU 2315750	C2	RU 2004-104628	20020715
MX 2004000272	A1	MX 2004-272	20040109
NO 2004000162	A	NO 2004-162	20040114
KR 2004029369	A	KR 2004-700679	20040116
US 20040214822	A1	US 2004-758241	20040116
ZA 2004001223	A	ZA 2004-1223	20040216
DE 50211466	G	DE 2002-50211466	20020715
DE 50211466	G	EP 2002-764691	20020715
DE 50211466	G	WO 2002-EP7849	20020715

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1406859	A1 Based on	WO 2003008371 A
AU 2002328894	A1 Based on	WO 2003008371 A
BR 2002011223	A Based on	WO 2003008371 A
HU 2004000207	A2 Based on	WO 2003008371 A
MX 2004000272	A1 Based on	WO 2003008371 A
JP 2005504742	W Based on	WO 2003008371 A
NZ 531112	A Based on	WO 2003008371 A
AU 2002328894	B2 Based on	WO 2003008371 A
EP 1406859	B1 Based on	WO 2003008371 A
RU 2315750	C2 Based on	WO 2003008371 A
DE 50211466	G Based on	EP 1406859 A
DE 50211466	G Based on	WO 2003008371 A

PRIORITY APPLN. INFO: DE 2001-10135635

20010717

AN 2003-267985 [26] WPIX
 AB WO 2003008371 A1 UPAB: 20060119

NOVELTY - 1,4-Disubstituted 4-aminocyclohexanol derivatives (I) are new.
 DETAILED DESCRIPTION - Aminocyclohexanol derivatives of formula (I) (including racemates and pure stereoisomers (specifically enantiomers or diastereomers) or their mixtures) and their salts (specifically hydrochlorides) and solvates (specifically hydrates) are new.

R1, R2, R5 = H, alkyl or cycloalkyl (both optionally unsaturated and optionally substituted), Ar or -Q-Cyc; or NR1R2 = morpholino, 4-(R5)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;
 Ar = aryl or heteroaryl (both optionally substituted); Q = 1-3C alkylene;
 Cyc = optionally substituted cycloalkyl or Ar; R3 = alkyl or cycloalkyl (both optionally unsaturated and optionally substituted), Ar or -Q'-Cyc; Q' = optionally unsaturated, optionally substituted 1-4C alkylene;
 R4 = Cyc, -CHR6(CH2)nR7, -C(Y)(CH2)nR7 or -R8-L-R9; n = 0-3;
 Y = O, S or H2;
 R6 = H, or 1-7C alkyl or 1-6C alkoxy carbonyl (both optionally unsaturated and optionally substituted); R7 = H or Cyc;
 R8 = Ar;
 L = CONH, NHCO, COO, OCO, O, S or SO2; and R9 = Ar;
 provided that: alkyl moieties have 1-8C and cycloalkyl moieties 3-8C unless specified otherwise; and R1 and R2 are not both H. An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Neuroprotective; Nootropic; Antiaddictive; Antialcoholic; Vasotropic; Cardiant; Hypotensive; Hypertensive; Auditory; Antipruritic; Antimigraine; Anorectic; Antidiarrheic; Immunomodulator; Urothatic; Relaxant; Antitussive; Anesthetic; Diuretic; Antidiuretic.

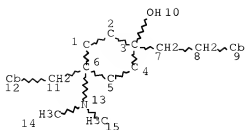
In a mouse tail-flick test for analgesic activity, 4-benzyl-4-dimethylamino-1-phenethyl- cyclohexanol (Ia) hydrochloride displayed an ED50 of 0.015 mg/kg when administered intravenously.

MECHANISM OF ACTION - Opioid-Like Receptor 1 Ligand (ORL1); nociceptin/ORL1 Receptor Modulator. In an ORL1 receptor binding assay, 4-benzyl -4-dimethylamino-1-phenethyl-cyclohexanol (Ia) hydrochloride displayed a Ki of 0.02 microM.

USE - (I) Are used: for treatment of pain (especially acute, visceral, neuropathic or chronic pain); for treatment of anxiety states, stress and associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory difficulties, withdrawal symptoms, alcohol, drug or medication abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, gastric motility deficiency, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence; as nootropic agents, muscle relaxants, anticonvulsants, antitussive agents or anesthetics; for coadministration with other opioid analgesics or with anesthetics; or for diuresis, antinatriuresis and/or anxiolysis (all claimed). (I) Are especially useful for treating pain.

ADVANTAGE - (I) Have high affinity for the ORL1 receptor and low toxicity.

L1 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

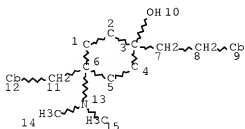
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

L2 14 SEA FILE=REGISTRY SSS FUL L1

L6 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 9 12

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

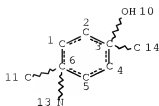
ECLEVEL IS LIM ON ALL NODES

ALL RING(S) ARE ISOLATED

L7 0 SEA FILE=MARPAT SSS SAM L6 (MODIFIED ATTRIBUTES)

L9

STR



NODE ATTRIBUTES:

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NSPEC   IS RC      AT   11
NSPEC   IS RC      AT   13
NSPEC   IS RC      AT   14
CONNECT IS X2      RC AT   1
CONNECT IS X2      RC AT   2
CONNECT IS X2      RC AT   4
CONNECT IS X2      RC AT   5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

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STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

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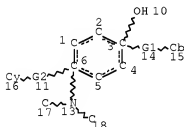
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

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L10 (      212)SEA FILE=MARPAT SSS FUL L9 (MODIFIED ATTRIBUTES)
L11      STR

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REP G1=(0-2) CH2

REP G2=(0-1) CH2

NODE ATTRIBUTES:

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NSPEC   IS RC      AT   13
CONNECT IS X2      RC AT   1
CONNECT IS X2      RC AT   2
CONNECT IS X2      RC AT   4
CONNECT IS X2      RC AT   5
DEFAULT MLEVEL IS ATOM
MLEVEL   IS CLASS  AT   15 16
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

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L12          7 SEA FILE=MARPAT SUB=L10 SSS FUL L11 (MODIFIED ATTRIBUTES)
              (FILE 'REGISTRY' ENTERED AT 10:58:22 ON 18 MAR 2008)
                ACT BROOK758/A
                -----
L1            STR
L2            14 SEA SSS FUL L1
                -----
                D QUE STAT

FILE 'CAPLUS' ENTERED AT 10:59:13 ON 18 MAR 2008
L3            1 SEA ABB=ON PLU=ON L2
                D IBIB ABS HITSTR

FILE 'CAOLD' ENTERED AT 10:59:31 ON 18 MAR 2008
L4            0 SEA ABB=ON PLU=ON L2

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 10:59:38 ON 18 MAR 2008
L5            0 SEA ABB=ON PLU=ON L2

FILE 'MARPAT' ENTERED AT 10:59:42 ON 18 MAR 2008
L6            STR L1
L7            0 SEA SSS SAM L6 (MODIFIED ATTRIBUTES)
L8            0 SEA SSS FUL L6 (MODIFIED ATTRIBUTES)
                ACT BROOKM/A
                -----
L9            STR
L10 (         212)SEA SSS FUL L9 (MODIFIED ATTRIBUTES)
L11            STR
L12            7 SEA SUB=L10 SSS FUL L11 (MODIFIED ATTRIBUTES)
                -----
                D QUE STAT L8
                D QUE STAT L12

FILE 'CAPLUS' ENTERED AT 11:11:17 ON 18 MAR 2008
L13            7 SEA ABB=ON PLU=ON L12
L14            6 SEA ABB=ON PLU=ON L13 NOT L3

FILE 'MARPAT' ENTERED AT 11:11:36 ON 18 MAR 2008
L15            6 SEA ABB=ON PLU=ON L14
                D 1-6

FILE 'REGISTRY' ENTERED AT 11:12:24 ON 18 MAR 2008
L16            31479 SEA ABB=ON PLU=ON ?CYCLOHEXANOL?/CNS
L17            113 SEA ABB=ON PLU=ON ?BENZYL-4-DIMETHYLAMINO?/CNS
L18            21 SEA ABB=ON PLU=ON L16(L) L17

FILE 'CAPLUS' ENTERED AT 11:15:17 ON 18 MAR 2008
L19            3 SEA ABB=ON PLU=ON L18
L20            35 SEA ABB=ON PLU=ON (4(W) (BENZYL OR BZ)) (1W) (DIMETHYLAMINO?
                OR DI(W) (METHYLAMINO? OR (ME OR METHYL) (W)AMINO?) OR

```


DIMETHYL AMINO?)
 L21 2 SEA ABB=ON PLU=ON L20(S) (?CYCLOHEXANOL? OR ?CYCLO
 HEXANOL?)
 L22 2 SEA ABB=ON PLU=ON (L19 OR L21) NOT L3
 D 1-2
 FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS' ENTERED
 AT 11:18:33 ON 18 MAR 2008
 L23 1 SEA ABB=ON PLU=ON L21
 D IBIB ABS

FILE 'HOME' ENTERED AT 11:20:17 ON 18 MAR 2008
 D QUE L2
 D QUE L7
 D QUE L12

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 MAR 2008 HIGHEST RN 1008496-49-8
 DICTIONARY FILE UPDATES: 17 MAR 2008 HIGHEST RN 1008496-49-8

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<http://www.cas.org/support/stngen/stdoc/properties.html>

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 FILE LAST UPDATED: 17 Mar 2008 (20080317/ED)

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FILE CAOLD
 FILE COVERS 1907-1966

10/758241

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE MEDLINE

FILE LAST UPDATED: 15 Mar 2008 (20080315/UP). FILE COVERS 1949 TO DA

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 12 March 2008 (20080312/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE

FILE COVERS 1974 TO 18 Mar 2008 (20080318/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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FILE MARPAT

FILE CONTENT: 1961-PRESENT VOL 148 ISS 11 (20080314/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2008027098 31 JAN 2008

DE 102006031752 10 JAN 2008
 EP 1881549 23 JAN 2008
 JP 2008021517 31 JAN 2008
 WO 2008021152 21 FEB 2008
 GB 2439172 19 DEC 2007
 FR 2903984 25 JAN 2008
 RU 2315659 27 JAN 2008
 CA 2593150 06 JAN 2008

Expanded G-group definition display now available.

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FILE WPIX

FILE LAST UPDATED: 13 MAR 2008 <20080313/UP>
 MOST RECENT THOMSON SCIENTIFIC UPDATE: 200818 <200818/DW>
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http://www.stn-international.de/stndatabases/details/epc_0801.zip

Supplement of all changed ECLA items:

http://www.stn-international.de/stndatabases/details/ecla_0802s.zi

FILE JAPIO

FILE LAST UPDATED: 3 MAR 2008 <20080303/UP>
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>>> GRAPHIC IMAGES AVAILABLE <<<

FILE PASCAL

FILE LAST UPDATED: 17 MAR 2008 <20080317/UP>
 FILE COVERS 1977 TO DATE.

10/758241

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